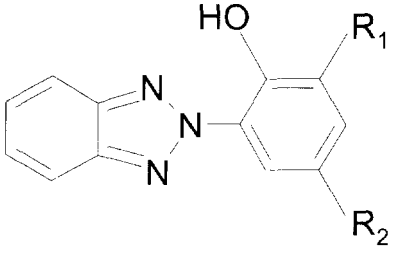
AR201-13266A

The Phenolic *Benzotriazoles* Association

High Production Volume (HPV) Challenge Program

Data Summary and Test Plan for Phenolic Benzotriazoles



September 15, 2001

Submitted to the EPA under the HPV Challenge Program by:

The Phenolic Benzotriazoles Association
(HPV Registration Number)

Contact Person: James Cooper
The Phenolic Benzotriazoles Association
1850 M Street, NW ▪ Suite 700
Washington, DC 20036
Tel: 202-72 I-41 58

Member Companies

Ciba Specialty Chemicals Corporation
540 White Plains Road
Tarrytown, NY 10591

Cytec Industries Inc.
Corporate Headquarters
Five Garret Mountain Plaza
West Paterson, NJ 07424

Table of Contents

THE PHENOLIC BENZOTRIAZOLE CATEGORY AND TEST PLAN

On November 29, 1999, The Phenolic Benzotriazole Association (PBA), whose members are Ciba Specialty Chemicals Corporation and Cytec Industries inc., voluntarily agreed to participate in the Environmental Protection Agency's High Production Volume Chemical Challenge Program. By participating in this program, PBA agreed to assess the adequacy of existing data, design and submit test plans to fill data gaps where necessary and appropriate, provide test results, and prepare summaries of the data characterizing each chemical sponsored.

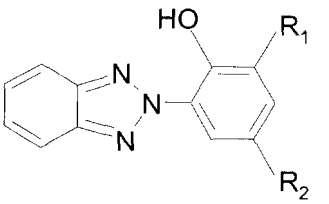
The sponsored chemicals addressed in this test plan are:

2-(2'-hydroxy-5'-methylphenyl) benzotriazole	CAS# 2440-22-4
2-(2'-hydroxy-5'-octylphenyl) benzotriazole	CAS# 3 147-75-9
2-(2'-hydroxy-3', 5'-di-t-amylphenyl) benzotriazole	CAS# 25973-55-l
2-(2H-benzotriazol-2-yl)-4,6-bis (1 -methyl-l -phenylethyl) phenol	CAS# 7032 1-86-7

Based on their structural, physical, chemical and toxicological similarities, these mono and di-substituted phenolic derivatives of the benzotriazoles are proposed as a category for the purposes of the HPV program.

Background Information

The Phenolic Benzotriazole category includes 4 compounds all of which have the identical molecular base structure of a benzotriazole group:



They also have in common a phenolic group attached to the benzotriazole structure at the same location but they vary in the substrates (R1 and R2) present on the phenolic group (also see Fig. 1).

These compounds are potent UV-light absorbers and constitute an important class of industrial additives for polymers and light-stabilized coatings. They are used in a variety of polymers including polycarbonates, unsaturated polyesters, polystyrenes, acrylics, polyvinyl chloride, thermoplastic polyesters, and polyacetals. The four substances have the common photochemical feature of strong absorption of ultraviolet light (290 - 350 nm). This feature, as an ultraviolet absorber (UVA), is utilized commercially to impart light stability (protection against photodegradation) to a wide variety of polymers and to coatings applied to numerous materials. The phenolic benzotriazole UV absorbers reduce or prevent the absorption of UV light by chromophores which in an excited state can form radicals that may have damaging effects on materials or alter their properties.

Compounds in this category are sold only to large industrial users as ingredients or reagents for their products and processes. There are no direct consumer applications for these compounds and no direct sales to the general public. FDA clearances for various uses in food contact polymers and adhesives are described in Table 1.

Table 1

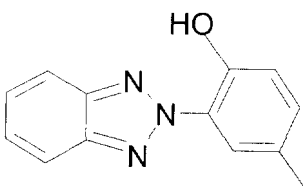
Summary of FDA Clearances for Phenolic Benzotriazoles

Chemical Name [CAS]	Food Additive Regulation	Uses
2-(2'-HYDROXY-5'-OCTYLPHENYL) BENZOTRIAZOLE [3147-75-9]	178.2010	Polycarbonate Resins complying with 177.1580
2-(2'-HYDROXY-5'-METHYLPHENYL) BENZOTRIAZOLE [2440-22-4]	178.2010	Polycarbonate Resins complying with 177.1580 Ethylene Phthalate Polymers complying with 177.1630 Ethylene-l ,4-cyclohexylene Dimethylene Terephthalate Copolymers complying with 177.1315 Polystyrene and Rubber-modified Polystyrene complying with 177.1640 Semirigid and Rigid Acrylic and Modified Acrylic Plastics complying with 177.1010 Rigid Polyvinyl Cchloride and/or Rigid Vinyl Chloride Copolymers complying with 177.1980
2-(2'-HYDROXY-3,5-DI-TERT-AMYLPHENYL) BENZOTRIAZOLE [25973-55-1]	175.105	Adhesives
2-(2H-BENZOTRIAZOL-2-YL)-4,6-bis(1-METHYL-1-PHENYLETHYL)PHENOL [70321-86-7]	178.2010	Polycarbonate Resins complying with 177.1580 Polyethylene Phthalate Polymers complying with 177.1630

Structural Classification

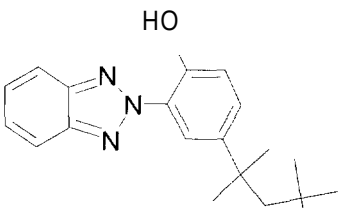
2-(2'-Hydroxy-5'-methylphenyl)benzotriazole (CAS # 2440-22-4), the simplest member of the present phenolic benzotriazole category, has a single methyl substrate para to the phenolic group. 2-(2'-Hydroxy-5'-octylphenyl)benzotriazole (CAS # 3147-75-9) is similar but has a branched butyl group at the para position. The other two compounds are 3, 5 di-substituted and branched derivatives of phenolic benzotriazoles.

Figure 1. Chemical Structure of Phenolic Benzotriazoles



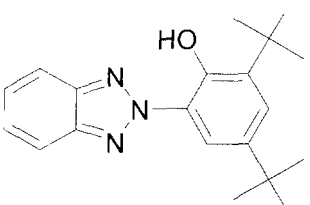
2-(2'-Hydroxy-5'-methylphenyl)-benzotriazole

CAS NO. 2440-22-4



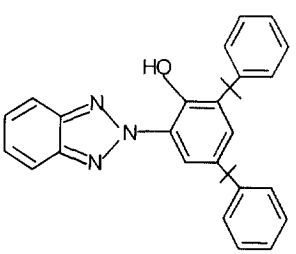
2-(2'-Hydroxy-5'-octylphenyl)-benzotriazole

CAS NO. 3147-75-g



2-(2'-Hydroxy-3', 5'-di-t-amylphenyl)-benzotriazole

CAS NO. 25973-55-I



2-(2H-Benzotriazol-2-yl)-4,6-bis(1 -methyl-l -phenylethyl)phenol

CAS NO. 70321-86-7

Toxicology of Benzotriazoles

Toxicologically, this class of chemicals is characterized by (1) low acute mammalian toxicity; (2) moderate toxicity with repeated exposure (effects typically in liver and kidney); (3) the lack of genotoxicity; (4) low toxicity to aquatic organisms. The compounds have similar environmental chemistry properties and a resistance to microbial biodegradation (Table 2).

Mammalian Toxicology. The acute oral LD50 for all four phenolic benzotriazoles was greater than 2 grams / kg hence they are relatively non-toxic with short-term exposure. 2-(2'-Hydroxy-5'-methylphenyl) benzotriazole and 2-(2H-benzotriazol-2-yl)-4,6-bis (1 -methyl-I-phenylethyl) phenol were tested for developmental toxicity in rodents, and reported to have NOELs of 1000 mg/kg and 3000 mg/kg, respectively. In a 30-day repeated dose toxicity study, 2-(2'-hydroxy-5'-octylphenyl) benzotriazole had relatively low toxicity, with a NOEL > 5658 mg/kg/day in the rat. However, insufficient details were available in the study to verify the conclusion that no organ weight or histopathological effects occurred. 2-(2'-Hydroxy-5'-methylphenyl) benzotriazole had a NOEL of 1000 ppm (32-35 mg/kg/day) in a 90-day dog study, with increased liver enzymes reported at higher dose levels. Carcinogenicity studies in both rats and mice for 2-(2'-Hydroxy-5'-methylphenyl) benzotriazole showed no significant increase in tumors related to dietary exposure to the chemical over the life-time of the animals. The di-substituted phenolic benzotriazoles had greater toxicity. 2-(2'-Hydroxy-3', 5'-di-t-amylphenyl) benzotriazole had NOELs of <100 ppm (22 mg/kg/day) and < 15 mg/kg in 90-day rat and dog studies, respectively. A 90-day study of 2-(2H-benzotriazol-2-yl)-4,6-bis (1 -methyl-I -phenylethyl) phenol in rats indicated a NOEL of 50 ppm. For both di-substituted phenolic benzotriazoles, the liver was the principal target organ, with histopathological changes, including hepatocellular hypertrophy and necrosis. Kidney toxicity was observed at higher dose levels. The common nature of the general toxicology findings with the investigated derivatives suggests a common basis of action.

Genetic Toxicology. None of the four compounds was mutagenic to bacteria in the Ames test. Of the two tested for chromosomal aberrations in vivo, neither was clastogenic.

Ecotoxicity. All four chemicals in this class exhibited low acute (96-hour) toxicity to fish,

with an LC50 > 67 ppm reported for 2-(2H-benzotriazol-2-yl)-4,6-bis (1-methyl-1-phenylethyl) phenol and LC50s > 100 ppm for the other three chemicals. In daphnia, the 24-hour EC50 was 15 ppm for 2-(2'-hydroxy-5'-octylphenyl) benzotriazole; the 24-hour EC50s for the other phenolic benzotriazoles in this class were higher with values ranging from > 91 ppm to >1000 ppm (Table 2). Toxicity testing with algae showed that the 72-hour EC50 for growth inhibition was > 10 ppm for 2-(2'-hydroxy-3', 5'-di-t-amylphenyl) benzotriazole, which was the highest concentration tested. The EC50s for 2-(2'-hydroxy-5'-octylphenyl) and 2-(2H-benzotriazol-2-yl)-4,6-bis (1 -methyl-l -phenylethyl) phenol were >100 ppm. Toxicity testing with algae are not available for 2-(2'-hydroxy-5'-methylphenyl) benzotriazole, however, the consistency of the low toxicity shown for the other benzotriazoles in this grouping indicates that algae are unlikely to be sensitive to this compound as well.

Physical Chemistry. The four chemicals in this class exhibited similar physical/chemical properties. Melting point temperatures ranged from 80 ^{o}C to 143 ^{o}C. The decomposition temperature was reported to be > 220 ^{o}C for 2-(2'-hydroxy-3', 5'-di-t-amylphenyl) benzotriazole and >350 ^{o}C for the other three phenolic benzotriazoles of this class. Vapor pressures, calculated using EPIWIN, all indicated a low volatility potential and ranged from 7.9 x 1 0^{-8} mm Hg for 2-(2'-hydroxy-5'-methylphenyl) benzotriazole to 1.6 x 1 0^{-14} mm Hg for 2-(2H-benzotriazol-2-yl)-4,6-bis (1 -methyl-l -phenylethyl) phenol. The compounds had partition coefficients ranging from 4.2 to 7.3, and low water solubility (< 1 mg/L). Hydrolysis could not be determined due to low solubility in water.

Environmental Fate. Photodegradation was predicted to be rapid, with half-lives ranging from 1.1 h to 8.1 h. Level III Fugacity models predicted these compounds to distribute primarily to soil and sediment. These compounds were not readily biodegradable. The biodegradability of 2-(2'-hydroxy-5'-methylphenyl) benzotriazole, 2-(2'hydroxy-3', 5'-di-t-amylphenyl) benzotriazole, and 2-(2H-benzotriazol-2-yl)-4,6-bis (l-Methyl -1 -phenylethyl) phenol, as indicated by the modified Sturm test, ranged from 0 to 8% after 28 days. 2-(2'-Hydroxy-5'-octylphenyl) benzotriazole was not biodegradable based on structure-activity analysis (EPIWIN).

DATA ADEQUACY AND TEST PLAN

Based on their structural similarities, the four phenolic benzotriazoles that comprise this class are expected to have similar physical, chemical, and biological properties. Review of the existing test data supports this view. The test data are fairly consistent among the four compounds. Where differences exist, the data generally lie within a range represented by 2-(2-hydroxy-5-methylphenyl)benzotriazole and 2-(2H-benzotriazol-2-yl)4,6-bis(1 -methyl)-1 -phenylethyl)phenol, the lowest and highest molecular weight compounds of this class. We propose to use these two chemicals to represent the category of phenolic benzotriazoles.

2-(2-hydroxy-5-methylphenyl)benzotriazole. Test data are complete with the exception of hydrolysis, toxicity to aquatic plants, and reproductive toxicity.

2-(2H-benzotriazol-2-yl)4,6-bis(1-methyl)-1-phenylethyl)phenol. Test data are complete with the exception of hydrolysis and reproductive toxicity.

New testing will be conducted for reproductive toxicity for these two chemicals. Based on the similarity of the compounds in this class, we believe that the data for 2-(2-hydroxy-5-methylphenyl)benzotriazole and 2-(2H-benzotriazol-2-yl) 4,6-bis(1-methyl)-1 - phenylethyl)phenol will be representative of the other chemicals in this category. Testing procedures will follow OECD guideline 421.

The low water solubility of these compounds makes it impractical to conduct hydrolysis studies, therefore, testing is not planned for hydrolysis. Aquatic plant testing is not planned for 2-(2-hydroxy-5-methylphenyl)benzotriazole because of the availability of algae test data for the other three compounds in the category and the overall low toxicity to algae demonstrated by this testing.

Table 2

Summary of Available Data for Phenolic Benzotriazole Category

SIDS Test	CAS 2440-22-4 2-(2-Hydroxy-5-methylphenyl)benzo-triazole Molecular Weight: 225.25	CAS 3147-75-9 2-(2-Hydroxy-5-tert-octylphenyl)benzo-triazole Molecular Weight: 323.44	CAS 25973-55-1 2-(2-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole Molecular Weight: 351.50	CAS 70321-86-7 2-(2H-Benzotrialzol-2-yl)-4,6-bis(1 -methyl-l. phenylethyl)phenol Molecular Weight: 447.58
Acute Mammalian	LD50 > 10,000 mg/kg	LD50 > 10,000 mgikg	LD50 >2325 mg/kg	LD50 >7750 mgikg
Repeat Dose	NOEL = 1000 ppm (Dog)	NOEL > 5,658 mg/kg/day (Rat)	NOEL < 100 ppm (Rat); < 15 mgikg (Dog)	NOEL = 50 ppm (Rat)
Point/gene Mutation	Negative (Ames)	Negative (Ames)	Negative (Ames)	Negative (Ames)
Chromosomal Aberration	Negative (3 *in vivo* studies)	No Data	No Data	Negative *(in vivo)*
Development/ Teratogenicity	NOEL = 1000 mg/kg (Rat, Mouse)	No Data	No Data	NOEL = 3000 mgikg (Rat)
Reproduction	No Data	No Data	No Data	No Data
Carcinogcnicity	No evidence of carcinogenicity in the rat or mouse after 24 months of dietary exposure to the test substance	No Data	No Data	No Data
Acute Fish	LC50 > 100 ppm	LC50 > 100 ppm	LC50 > 100 ppm	LC50 > 67 ppm
Gcutc Daphnia	EC50 > 1,000 ppm	EC50 = 15 ppm	EC50 > I 00 ppm	EC50 > 9 l ppm
Algae Growth Inhibition	No Data [1]	EC50 >100 ppm	EC50 > 10 ppm	EC50 > 100 ppm

Based on data from the other benzotriazoles in the category the EC50 is estimated to be > 100 ppm.

Table 2 (Continued)

Photodcgradation	T1/2 = 1.39 hours (*)	T1/2 = 4.02 h (*)	T1/2 = 8.1 h (*)	T1/2 = 1.06 h (*)
Water Stability / hydrolysis	No Data'	No Data	No Data	No Data'
Fugacity Calculation (*)	Air 3.1% Water 4.9% Soil 87.3% Sediment 4.6%	Air 4.0 x 10^{-5}% Water 3.5% Soil 44.6% Sediment 5 1.9%	Air 2.3 x 10^{-4}% Water 2.2% Soil 40.4% Sediment 57.5%	Air 0% Water 2.2% Soil 40.1% Sediment 57.7%
Biodegradation	Not readily biodegradable (measured)	Not readily biodegradable (measured)	Not readily biodegradable (measured)	Not readily biodegradable (measured)
Melting Point	131-133 °C (measured)	106 - 108 °C (measured)	80 - 83 °C (measured)	139-143 °C (measured)
Boiling Point	225 °C (measured)	N/A	477.8 °C (*)	599.8 °C (*)
Water Solubility	< 1 mg/L (measured)	< 1 mg/L (measured) 0.168 mg/L (*)	0.0 15 mg/L (*)	0.04 mg/L (measured) 0.0097 mg/L (*)
Log P	4.2 (measured)	6.2 (*)	7.3 (*)	> 6.5 (measured) 7.2 (*)
Vapor Pressure	7.94 x 10^{-8} mm Hg (*)	1.1 x 10^{-9} mm Hg (*)	1.93 x 10^{-10} mm Hg (*)	1.62 x 10^{-14} mm Hg (*)

The low water solubility of these compounds makes it impractical to conduct hydrolysis studies.

* Estimated Value using EPIWIN Model (Syracuse Research Corporation, 2000)